

## Application Serial No. 10/086,805

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Withdrawn) An apparatus for identifying molecular structures within a sample substance, comprising:

an integrated circuit array sensor for outputting signals representative of the interaction of probe molecular structures on the surface of said sensor and target molecular structures within a sample substance (hereinafter "target");

a controller unit for interfacing with said integrated circuit array sensor and accessing said signals representative of the interaction of probe and target molecular structures;

an input/output port for communicating with control, post-processing, and data storage circuit;

a chamber, such as a hybridization chamber, for exposing sensitive area of said integrated array sensor to the sample substance; and

a means for controlling and programmable changing of the temperature of said chamber, the sample substance and said integrated array sensor.

2. (Withdrawn) The integrated array sensor of claim 2, where said sensor comprises a set of pixel circuits, each said pixel is usually not bigger than (1 mm x 1 mm) in size, and most preferably is less than (100  $\mu$ m x 100  $\mu$ m) in size;

each said pixel is capable of accumulating and processing an electric charge produced upon interaction of probe and target molecular structures on the surface of said sensor.

3 (Withdrawn) The integrated array sensor of claim 1, where said sensor comprises an array of active pixels, each said pixel has one or more active transistors within the pixel unit, and each said pixel has a connection with a multiple column readout circuit, similar to the architecture implemented by Complementary Metal Oxide Semiconductor (CMOS) array imagers. Said active pixels are capable of converting the electric charge accumulated by said pixels into an output electronic signal.

4. (Withdrawn) Alternatively, the integrated array sensor of claim 1, where said sensor comprises an array of pixels capable of accumulating, storing, and transferring an electric charge to a readout register formed in the sensor's substrate, similar to the design

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implemented by a Charge-Coupled Device (CCD). Said pixels and readout circuits are capable of converting an electric charge accumulated by said pixels into an output electronic signal.

5. (Withdrawn) The chamber of claim 1, where said chamber is attached thereto to the sensitive area of said integrated array sensor such that filling said chamber with a sample substance exposes the sensitive area of the integrated array sensor to that sample substance.

6. (Withdrawn) The means for controlling and changing temperature of claim 1, where said means allows maintaining a constant preprogrammed temperature of the sample substance and said integrated array sensor, or alternatively, said means allows running a preprogrammed change of temperature versus time such as, for example, gradually increasing or decreasing the temperature, or a stepwise change of temperature. Said means for controlling and changing temperature also are capable of providing an electronic output versus time representative of the temperature of the sample substance and the integrated array sensor.

7. (Currently amended) A method for identifying molecular structures within a sample substance, comprising the steps of:

- (a) applying the substance to a plurality of test sites formed on a surface of said an integrated circuit array sensor, wherein the integrated array sensor includes a set of active pixels, with each pixel having one or more transistors within the pixel and multiple column readout circuits and is operable to detect and output an electrical signal representative of the electric charge accumulated by associated pixel circuitry upon formation or dissociation of molecular complexes formed on said test sites of the array sensor, and wherein said test sites having respective probes attached thereto which specifically bind to a target molecular structure, such that different test sites have probes which specifically bind to different target molecular structures;
- (b) controlling the maintaining a constant preprogrammed temperature of the substance and said integrated circuit array sensor, or alternatively, running a preprogrammed temperature profile such as, but not limited to, gradually increasing or decreasing the

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~~temperature or, stepwise changing of the temperature of the sample substance and said integrated array sensor;~~

- (c) acquiring an electronic signal from a plurality of the pixels associated with the test sites, each test site covering at least one pixel of said integrated array sensor; and
- (d) detecting the amplitude of the electronic signals versus time from the test sites to determine which probes have interacted with an associated target molecular structure such that a plurality of different targets can be detected.

8. (Currently amended) The method of claim 7 wherein said probes are oligonucleotide probes ~~or their analogous equivalent known to one skilled in the art.~~

Claims 9-11 (Withdrawn)

- 12. (Original) The method of claim 7 wherein said detection step comprises detecting an electronic signal at a constant temperature of the sample substance and said integrated array sensor.
- 13. (Original) The method of claim 7 wherein said detection step comprises detecting an electronic signal during a stepwise change of the temperature of the sample substance and said integrated array sensor.
- 14. (Currently amended) The method of claim 7 wherein said detection step comprises detecting an electronic signal during a ~~gradual~~ change of the temperature of the sample substance and said integrated array sensor.
- 15. (Original) The method of claim 7 wherein said detection step comprises detecting an electronic signal versus time for each probe site, therefore providing identification of the sample substance based upon the rate of a rising or falling electronic signal versus time due to forming or, equally acceptable, breaking of probe-target duplexes of the probe and target molecular structures.
- 16. (Original) The method of claim 14 wherein said detection step comprises detecting an electronic signal for each probe site versus the temperature, therefore providing said

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identification of the molecular structures of the sample substance based on the specific temperature of binding, or equally acceptable, based on the specific temperature of melting of probe-target duplexes.

17. (New) The method of claim 7, wherein the step of controlling the temperature of the substance and said integrated circuit sensor comprises maintaining a constant preprogrammed temperature of the substance and said integrated circuit array sensor.
18. (New) The method of claim 7, wherein the step of controlling the temperature of the substance and said integrated circuit sensor comprises increasing or decreasing the temperature of the substance and sensor as a function of time.
19. (New) The method of claim 7, wherein the step of controlling the temperature of the substance and said integrated circuit sensor comprises stepwise changing of the temperature of the sample substance and said integrated array sensor.
20. (New) A method for identifying molecular structures within a sample substance, comprising the steps of:
  - (a) applying the substance to a plurality of test sites formed on a surface of an integrated circuit array sensor, the integrated array sensor operable to detect electrical signals produced on the test sites in the absence of any external application of external electrical signals to the test sites, the test sites having respective probes attached thereto which specifically bind to a target molecular structure, such that different test sites have probes which specifically bind to different target molecular structures;
  - (b) controlling the temperature of the substance and said integrated circuit array sensor;
  - (c) acquiring an electronic signal from a plurality of the pixels associated with the test sites, each test site covering at least one pixel of said integrated array sensor; and
  - (d) detecting, in the absence of any external application of external electrical signals to the test sites, the amplitude of the electronic signals versus time from the test sites to determine which probes have interacted with an associated target molecular structure such that a plurality of different targets can be detected.